

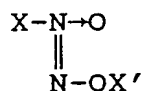
We claim:

1. A polymeric composition capable of releasing nitric oxide under physiological conditions, said composition comprising a biopolymer and a nitric oxide-releasing N_2O_2^- functional group bound to said biopolymer.

2. The polymeric composition of claim 1, wherein said biopolymer is selected from the group consisting of a peptide, polypeptide, protein, oligonucleotide, and nucleic acid.

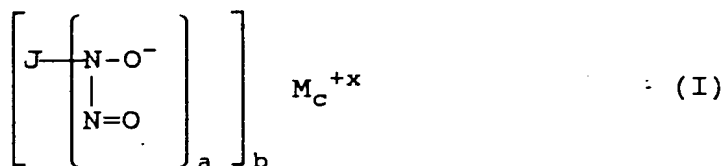
3. The polymeric composition of claim 2, wherein said biopolymer is selected from the group consisting of a tissue-, cell-, or tumor-specific antibody or fragment thereof, a protein containing a recognition sequence for a receptor-ligand interaction favorable to tumor cell attachment, an anti-chemotactic agent, and a hormone.

4. The polymeric composition of claim 1, wherein said nitric oxide-releasing N_2O_2^- group is of the formula



wherein X is an organic or inorganic moiety and X' is selected from the group consisting of X, a pharmaceutically acceptable metal center or a pharmaceutically acceptable cation, and wherein said N_2O_2^- group is bonded to said biopolymer through at least one of X or X'.

5. The polymeric composition of claim 4, wherein said nitric oxide-releasing N_2O_2^- functional group is of the formula:

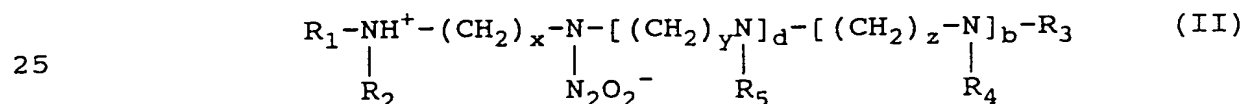


5 wherein J is an organic or inorganic moiety, M^{+x} is a pharmaceutically acceptable cation, where x is the valence of the cation, a an integer of at least one, and b and c are the smallest integers that result in a neutral compound.

15 6. The method of claim 5, wherein J is a moiety which is linked to the nitrogen of the remainder of the complex through an atom other than a carbon atom.

7. The polymeric composition of claim 5, wherein the nitric-oxide releasing group is a compound other than a salt of alanosine or dopastin.

20 8. The polymeric composition of claim 4, wherein said nitric oxide-releasing N_2O_2^- functional group is of the formula:



30 wherein b and d are the same or different and may be zero or one, R_1 , R_2 , R_3 , R_4 , and R_5 are the same or different and may be hydrogen, C_{3-8} cycloalkyl, C_{1-12} straight or branched chain alkyl, benzyl, benzoyl, phthaloyl, acetyl, trifluoroacetyl, p-toluyyl, t-butoxycarbonyl, or 2,2,2-trichloro-t-butoxycarbonyl, and

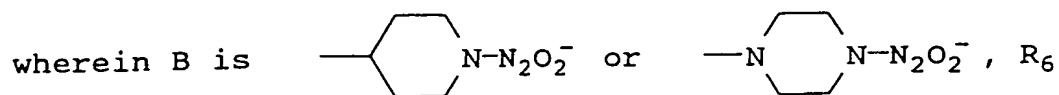
35 x, y, and z are the same or different and are integers from 2 to 12.

9. The polymeric composition of claim 4, wherein said nitric oxide-releasing N_2O_2^- functional group is of the formula:

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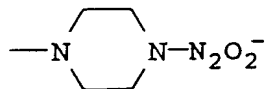


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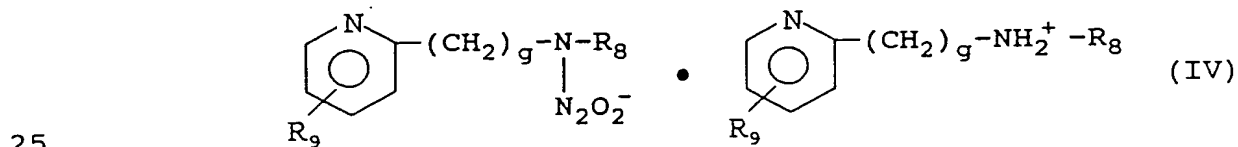
and R₇ are the same or different and may be hydrogen,
 10 C₃₋₈ cycloalkyl, C₁₋₁₂ straight or branched chain alkyl,
 benzyl, benzoyl, phthaloyl, acetyl, trifluoroacetyl, p-
 toluyl, t-butoxycarbonyl, or 2,2,2-trichloro-t-
 butoxycarbonyl, f is an integer from 0 to 12, with the
 proviso that when B is the substituted piperazine moiety

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then f is an integer from 2 to 12.

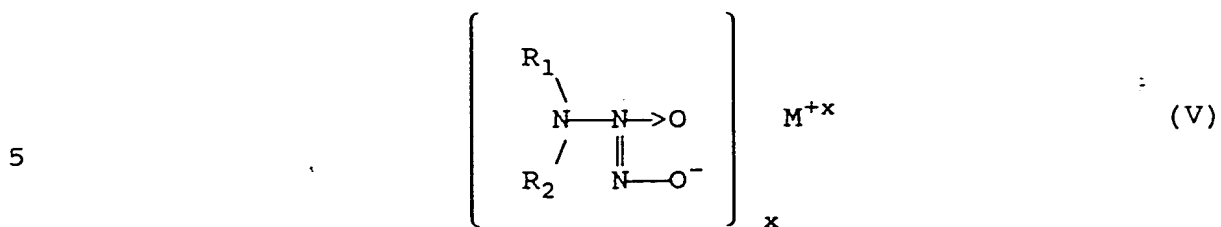
10. The polymeric composition of claim 4, wherein
 20 said nitric oxide-releasing N₂O₂⁻ functional group is of
 the formula:



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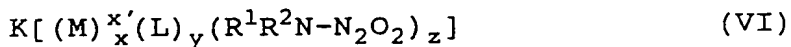
wherein R₈ is hydrogen, C₃₋₈ cycloalkyl, C₁₋₁₂ straight or
 branched chain alkyl, benzyl, benzoyl, phthaloyl,
 30 acetyl, trifluoroacetyl, p-toluyl, t-butoxycarbonyl, or
 2,2,2-tri-chloro-t-butoxycarbonyl, R₉ is hydrogen or a
 C₁-C₁₂ straight or branched chain alkyl, and g is 2 to 6.

11. The polymeric composition of claim 4, wherein
 35 said nitric oxide-releasing N₂O₂⁻ functional group is of
 the formula:



wherein R_1 and R_2 are independently selected from the group consisting of a straight chain or branched chain $C_1 - C_{12}$ alkyl group and a benzyl group, or else R_1 and R_2 together with the nitrogen atom they are bonded to form a heterocyclic group, a pyrrolidino, piperidino, piperazino or morpholino group, M^{+x} is a pharmaceutically acceptable cation, and x is the valence of the cation.

12. The polymeric composition of claim 4, wherein said nitric oxide-releasing $N_2O_2^-$ functional group is of the formula:



wherein M is a pharmaceutically acceptable metal, or, where x is at least two, a mixture of two different pharmaceutically acceptable metals, L is a ligand different from $(R^1R^2N-N_2O_2)$ and is bound to at least one metal, R^1 and R^2 are each organic moieties and may be the same or different, x is an integer of from 1 to 10, x' is the formal oxidation state of the metal M , and is an integer of from 1 to 6, y is an integer of from 1 to 18, and where y is at least 2, the ligands L may be the same or different, z is an integer of from 1 to 20, and K is a pharmaceutically acceptable counterion to render the compound neutral to the extent necessary.

13. The polymeric composition of claim 4, wherein said nitric oxide-releasing $N_2O_2^-$ functional group is of the formula:



wherein R is C₂₋₈ lower alkyl, phenyl, benzyl, or C₃₋₈ cycloalkyl, any of which R groups may be substituted by one to three substituents, which are the same or
 5 different, selected from the group consisting of halo, hydroxy, C₁₋₈ alkoxy, -NH₂, -C(O)NH₂, -CH(O), -C(O)OH, and -NO₂, X is a pharmaceutically acceptable cation, a pharmaceutically acceptable metal center, or a
 10 pharmaceutically acceptable organic group selected from the group consisting of C₁₋₈ lower alkyl, -C(O)CH₃, and -C(O)NH₂, and y is one to three, consistent with the valence of X.

14. The polymeric composition of claim 4, wherein
 15 said nitric oxide-releasing N₂O₂⁻ functional group is of the formula:



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wherein R₁ and R₂ are independently chosen from C₁₋₁₂ straight chain alkyl, C₁₋₁₂ alkoxy or acyloxy substituted straight chain alkyl, C₂₋₁₂ hydroxy or halo substituted
 25 straight chain alkyl, C₃₋₁₂ branched chain alkyl, C₃₋₁₂ hydroxy, halo, alkoxy, or acyloxy substituted branched chain alkyl, C₃₋₁₂ straight chain olefinic and C₃₋₁₂ branched chain olefinic which are unsubstituted or substituted with hydroxy, alkoxy, acyloxy, halo or
 30 benzyl, or R₁ and R₂ together with the nitrogen atom to which they are bonded form a heterocyclic group, a pyrrolidino, piperidino, piperazino or morpholino group, and R₃ is a group selected from C₁₋₁₂ straight chain and C₃₋₁₂ branched chain alkyl which are unsubstituted or
 35 substituted by hydroxy, halo, acyloxy or alkoxy, C₂₋₁₂ straight chain or C₃₋₁₂ branched chain olefinic which are unsubstituted or substituted by halo, alkoxy, acyloxy or hydroxy, C₁₋₁₂ unsubstituted or substituted acyl, sulfonyl and carboxamido; or R₃ is a group of the

formula $-(CH_2)_n-ON=N(O)NR_1R_2$, wherein n is an integer of 2-8, and R_1 and R_2 are as defined above; with the proviso that R_1 , R_2 and R_3 do not contain a halo or a hydroxy substituent α to a heteroatom.

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15. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 1.

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16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 2.

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17. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 3.

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18. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 4.

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19. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 5.

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20. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 6.

21. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 7.

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22. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 8.

23. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 9.

5 24. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 10.

10 25. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 11.

15 26. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 12.

20 27. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering to said mammal the polymeric composition of claim 1 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

25 28. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 2 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

30 29. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 3 in an amount sufficient to
35 release a therapeutically effective amount of nitric oxide.

30. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 4 in an amount sufficient to
5 release a therapeutically effective amount of nitric oxide.

31. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is
10 therapeutic, comprising administering the polymeric composition of claim 5 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

32. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is
15 therapeutic, comprising administering the polymeric composition of claim 6 in an amount sufficient to release a therapeutically effective amount of nitric
20 oxide.

33. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is
25 therapeutic, comprising administering the polymeric composition of claim 7 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

34. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is
30 therapeutic, comprising administering the polymeric composition of claim 8 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

35. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is

therapeutic, comprising administering the polymeric composition of claim 9 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

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36. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 10 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

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37. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 11 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

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38. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 12 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

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